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TITLE: Methods of modulating angiogenesis by regulating the expression of pituitary

tumor transforming gene (PTTG)

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INVENTOR-INFORMATION:

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RELATED-US-APPL-DATA:

Application 09/777422 is a continuation-in-part-of US application 09/730469, filed

December 4, 2000, PENDING

Application 09/730469 is a continuation-in-part-of US application 09/687911, filed October 13, 2000, PENDING

Application 09/687911 is a continuation-in-part-of US application 09/569956, filed May 12, 2000, PENDING

Application 09/569956 is a continuation-in-part-of US application 08/894251, filed July 23, 1999, PENDING

Application 08/894251 is a a-371-of-international WO application PC/T/US97/21463, filed November 21, 1997, UNKNOWN

Application is a non-provisional-of-provisional application 60/031338, filed November 21, 1996,

INT-CL: [07] A61 K 31/70, A01 N 43/04

US-CL-PUBLISHED: 514/44 US-CL-CURRENT: 514/44

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

Disclosed is a method of modulating angiogenesis in a tissue comprising mammalian cells, including cells of human origin, in vitro or in vivo. Also disclosed are a method of enhancing wound healing and/or tissue regeneration and a method of limiting scar formation.

[0001] This application is a continuation-in-part of U.S. Ser. No. 09/730,469, filed Dec. 4, 2000, which is a continuation-in-part of U.S. Ser. No.09/687,911, filed on Oct. 13, 2000, which is a continuation-in-part of U.S. Ser. No.09/569,956, filed on May 12, 2000, which is a continuation-in-part of U.S. Ser. No. 08/894,251, filed on Jul. 23, 1999, as a national stage application, under 35 U.S.C. .sctn.371, of international application PCT/US97/21463, filed Nov. 21, 1997, which claims the priority of the filing date of U.S. Provisional Application Serial No. 60/031,338, filed Nov. 21, 1996.

(FILE 'HOME' ENTERED AT 16:31:08 ON 16 OCT 2002) FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:31:19 ON 16 OCT 2002 2 S PTTG-C L10 S PITUITARY (W) TUMOR (5A) CARBOXY-TERMINAL L20 S PTTG(W)CARBOXY-TERMINAL L3 L42 DUP REM L1 (0 DUPLICATES REMOVED) => d bib ab 1-2 14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS L4AN2001:851202 CAPLUS 136:4255 DN ΤI C-terminal peptides of the PTTG gene product and their use in inhibition of neoplastic cellular proliferation or transformation IN Horwitz, Gregory A.; Zhang, Xun; HeaneyAnthony, P.; Melmed, Shlomo PA Cedars-Sinai Medical Center, USA SO PCT Int. Appl., 190 pp. CODEN: PIXXD2 DT Patent LA English FAN.CNT 6 PATENT NO. KIND DATE APPLICATION NO. DATE ----PΙ WO 2001087934 **A2** 20011122 WO 2001-US15254 20010512 WO 2001087934 **A3** 20020530 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002147162 A1 20021010 US 2001-777422 20010205 PRAI US 2000-569956 20000512 Α US 2000-687911 Α 20001013 US 2000-730469 Α 20001204 US 2001-777422 Α 20010205 US 1996-31338P P 19961121 WO 1997-US21463 W 19971121 US 1999-894251 A2 19990723 AB A method of inhibiting neoplastic cellular proliferation and transformation of mammalian cells using C-terminal peptides derived from the product of the PTTG (pituitary tumor transforming gene) gene is described. The peptides regulate the function of the protein and gene expression in a dominant neg. manner. The peptides may be used directly, as fusion proteins with uptake-promoting peptides, or expression vectors encoding the peptides may be used in gene therapy. The peptides may also increase the effectiveness of cytotoxic chemotherapeutic agents conventionally used to treat breast or ovarian cancers, thus allowing lower EDs of the agents to be administered. Kits comprising the inventive compns. are also disclosed for the treatment of neoplastic cellular proliferation in vitro or in vivo. Isolated PTTG-C

peptides and PTTG-C-related polynucleotides are also

disclosed, as are anti-PTTG-C-specific antibodies. Cloning and characterization of the PTTG gene and its role in neoplastic transformation is described. Two-hybrid assays showed that the PTTG gene product acted as a transcriptional activator. Deletion anal. identified the C-terminal region as important in regulating neoplastic transformation. This area is proline-rich and includes an SH3 domain. ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS 2001:850858 CAPLUS AN DN 136:4254 Pituitary tumor transforming gene 2 (PTTG2) and its role in the ΤI regulation of expression of pituitary tumor transforming gene 1 Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo IN PA Cedars-Sinai Medical Center, USA PCT Int. Appl., 175 pp. SO CODEN: PIXXD2 DT Patent LA English FAN.CNT 6 PATENT NO. KIND DATE APPLICATION NO. DATE _ _ _ _ --------------------PΙ WO 2001087039 A2 20011122 WO 2001-US15255 20010512 WO 2001087039 Α3 20020321 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002147162 A1 20021010 US 2001-777422 20010205

US 1999-894251 A2 19990723
WO 2001-US15255 W 20010512

AB Disclosed is a method of inhibiting neoplastic cellular proliferation and/or transformation of mammalian breast or ovarian cells, including cells of human origin, in vitro or in vivo. The inventive method involves

the use of pituitary tumor transforming gene 2 (PTTG2) product, which has the ability to regulate endogenous PTTG1 expression in a dominant neg. manner. In some embodiments, the invention is directed to gene-based treatments that deliver PTTG2-encoding polynucleotides to mammalian cells.

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whether in vitro or in vivo, to inhibit the endogenous expression of PTTG1. Other embodiments are directed to peptide-based treatments that deliver PTTG2 peptide mols. to the cells, which inhibit endogenous PTTG1 expression and/or PTTG1 function. Kits useful in practicing the inventive

method are also disclosed.

AU 2001063059

US 2000-569956

US 2000-687911

US 2001-777422

US 1996-31338P

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